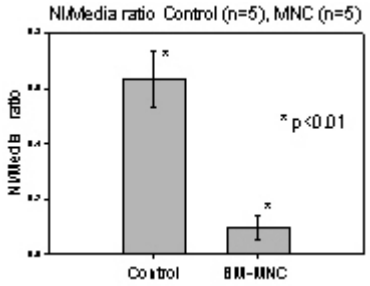
1064-188 **Bone Marrow Mononuclear Cell Therapy Reduces Post-Angioplasty Neointimal Formation in Rabbits**

Enrikas Vainorius, Brad S. Sutton, Yoshihisa Morimoto, Bryce H. Davis, Doris A. Taylor, Duke University, Durham, NC

Background: Bone marrow (BM) contains a population of multipotent mononuclear cells (MNCs) that are thought to play a role in vasculogenesis and wound repair. Neointimal hyperplasia after vascular injury represents a failure in wound repair. Thus we hypothesize that IV delivery of MNCs will reduce neointimal formation after experimental angioplasty.
Methods: Cholesterol-fed NZW rabbits underwent endothelial denudation by a balloon catheter in the right external iliac artery. Half the animals underwent BM biopsy to harvest MNCs. Within one hour after injury, 2-4 x 10^6 cells (MNCs, n=5) or vehicle (Control, n=5) were injected intravenously. At 4 weeks, arteries were harvested.
Results: Morphometric analysis revealed significantly less neointima (NI) (0.048±0.022 mm^2 vs. 0.377±0.057 mm^2, p<0.01) and decreased NI/media ratios in MNC versus control animals (Figure 1). Medial area did not differ significantly in these two groups (MNCs 0.597±0.05 mm^2 vs. Control 0.638±0.06 mm^2). Immunohistochemistry revealed decreased macrophage and inflammatory cell activity in the vessel wall after MNCs as compared to Controls. Both groups exhibited smooth muscle cell infiltration in the neointima and complete re-endothelialization.
Conclusions: Acute, intravenous administration of MNCs decreases neointimal formation after balloon arterial (endothelial) injury. The ability of MNCs to modulate local macrophage and leukocyte accumulation within the vessel wall may explain the observed benefit.



POSTER SESSION

1065

Determinants of Endothelial Dysfunction and Response to Treatment

Monday, March 08, 2004, 9:00 a.m.-11:00 a.m.
Morial Convention Center, Hall G
Presentation Hour: 9:00 a.m.-10:00 a.m.

1065-165 **Brachial Artery Flow-Mediated Vasodilation Correlates With Exercise Capacity in Women**

Ayan R. Patel, Jeffrey T. Kuvin, Kathleen A. Sliney, William M. Rand, Natesa G. Pandian, Richard H. Karas, Tufts-New England Medical Center, Boston, MA

Background. Vascular endothelial dysfunction is present in individuals with atherosclerosis, and is a predictor of cardiac events in these patients. Prior work has demonstrated that peripheral vascular endothelial function correlates with exercise capacity (also a prognostic indicator in coronary disease) in predominantly male populations. However, whether peripheral vascular endothelial function correlates with exercise capacity in women is unknown. The purpose of this study was to determine whether brachial artery flow-mediated vasodilation (FMD) correlates with exercise capacity in women. **Methods.** 123 women referred for clinically-indicated stress testing underwent symptom-limited, Bruce protocol exercise treadmill testing with myocardial perfusion imaging. Brachial artery ultrasound imaging was performed under standard conditions. FMD was defined as the percent change in brachial artery diameter during reactive hyperemia compared to baseline. The presence of coronary artery disease (CAD) was defined as an abnormal sestamibi scan confirmed by prior or subsequent angiography. **Results.** There was a significant correlation between exercise treadmill time (ETT) and FMD (r=0.307, p<0.001). Using the median FMD value of 11% as a cut-point, subjects with an FMD>=11% had a significantly higher ETT (492±18 sec (mean ± SEM); n=62) than those with FMD<11% (410±16 sec; n=61; p<0.001). The correlation between FMD and ETT was present even when subjects with CAD were excluded (n=105, r=0.34, p<0.001). Partial correlation analysis demonstrated that the relationship between FMD and ETT remained significant when additional variables of age and left ventricular ejection fraction were considered. **Conclusion.** Brachial artery FMD correlates with exercise treadmill time in women, even in the absence of CAD. These findings suggest that endothelium-dependent regulation of vasomotor tone may play a role in determining exercise capacity, and further that loss of normal endothelial function may contribute to impaired exercise capacity in women. Future studies will be needed to determine whether interventions that improve endothelial function also enhance exercise capacity in women.

1065-166 **Added Ramipril to Simvastatin Shows Additive Effects on Flow-Mediated Dilation and Inflammation Markers in Diabetic and Hypercholesterolemic Patients: A Randomized, Double-Blind, Placebo-Controlled, Crossover Study**

Kwang K. Koh, Seung H. Han, Jeong Y. Ahn, Wook-Jin Chung, Woong C. Kang, Mi-Seung Shin, Eak K. Shin, Gachon Medical School, Incheon, South Korea

Background: Because the mechanisms of the biological effects of statins and antiotensin converting enzyme inhibitor therapies differ, we studied the vascular responses to these therapies in diabetic and hypercholesterolemic patients.
Methods: We administered simvastatin 20 mg and placebo or ramipril 10 mg daily during 2 months with washout 2 months to 30 diabetic and hypercholesterolemic patients. This study was randomized, double-blind, placebo-controlled, crossover in design. *=P<0.05;**=P<0.01;***=P<0.001 vs. Baseline. Data= mean±SEM or median (25%-75%).
Results: Simvastatin alone or ramipril combined with simvastatin significantly changed lipoproteins, and improved the percent flow-mediated dilator response (FMD) to hyperemia by 52±7% and by 73±10%, respectively (both P<0.001) and reduced serum levels of C-reactive protein (CRP) by 9% and by 25%, respectively (P=0.034 and P<0.001, respectively), compared with baseline measurements. Both therapies did not significantly change the percent nitroglycerin-induced dilator response (NTG). There were no significant correlations between the percent changes in lipoprotein or CRP levels and the percent changes in FMD after each therapy. Of interest, ramipril combined with simvastatin changed FMD and CRP levels to greater extent than simvastatin alone (P=0.003 and P=0.184, respectively),.
Conclusions; Compared with simvastatin alone, added ramipril to simvastatin showed additive effects on flow-mediated dilation and inflammation marker in diabetic and hypercholesterolemic patients.
Baseline1 Statin+Placebo Baseline2 Statin+Ramipril
TC (mg/dl) 246±8 171±6*** 240±9 174±7***
TG (mg/dl) 231±41 163±17* 238±26 186±23***
HDL-C (mg/dl) 49±2 47±2 49±2 51±2
LDL-C (mg/dl) 150±8 82±6*** 147±8 88±7***
Apo A-I (mg/dl)150±5 156±4 156±7 164±5
Apo B (mg/dl) 131±6 87±4*** 127±5 90±4***
FMD (%) 4.60±0.22 6.72±0.24*** 4.51±0.20 7.44±0.26***
NTG (%) 12.61±0.62 13.32±0.68 12.84±0.63 13.40±0.70
CRP (mg/dl) 0.19 (0.11-0.44) 0.12 (0.11-0.25)* 0.18 (0.10-0.64) 0.14 (0.11-0.20)***

1065-167 **Impaired Endothelial Function Correlates With Coronary Calcification in Asymptomatic Perimenopausal Women**

Steven M. Hollenberg, Andrew Dumasius, Vijay K. Verma, Hillary Maitland, Kim Sutton-Tyrrell, Karen Matthews, Lynda Powell, Cooper Hospital, Camden, NJ

Background: Elevations in coronary artery calcification (CAC) scores detected by electron beam computed tomography (EBCT) correlate with the extent of atherosclerosis. The degree of brachial artery flow-mediated dilation (FMD) after reactive hyperemia is dependent on intact endothelial function. We evaluated the correlation between endothelial dysfunction and CAC in asymptomatic perimenopausal women enrolled in the SWAN-Heart study.
Methods: 213 women underwent EBCT and assessment of brachial FMD; studies were done fasting and off medications and tobacco. High resolution ultrasound was used to measure brachial artery diameter before and after upper arm occlusion for 5 minutes. Images captured on each r wave for 180 sec, and FMD analyzed with proprietary software. CAC scores were divided into 3 groups: <10 (no significant calcium), 10-50, and >50.
Results: Mean age was 49.9, MAP 95.0, BMI 29.1; 5% were smokers. Mean CAC was 8.1. Mean FMD was 6.1%. FMD decreased in a graded fashion with increasing CAD (6.5±3.9 <10, 5.3±3.7 10-50, 3.4±2.3 >50, p<0.05 by ANOVA). There were no significant differences between groups in BP, age, lipids, or other cardiac risk factors.
Conclusions: In this population of asymptomatic perimenopausal women, elevated CAC scores correlated with impaired endothelial function. High CAC scores have previously been shown to predict subsequent cardiac events in asymptomatic subjects. The graded correlation between FMD and CAC in perimenopausal women suggests a role for endothelial dysfunction in the development of subclinical atherosclerosis in this group.

1065-168 **Recovery of Impaired Microvascular Function in Collateral-Dependent Myocardium After Recanalization of a Chronic Total Coronary Occlusion**

Gerald S. Werner, Markus Ferrari, Ralf Surber, Philipp Bahrmann, Gero Schwarz, Hans R. Figulla, Friedrich-Schiller-University, Jena, Germany

Background. From studies on the recanalization of acute occlusions it is known that an impaired microvascular function may impede the recovery of LV function. It is yet unknown whether microvascular function would affect the recovery of LV function in chronic total coronary occlusions (CTOs) of longer duration. This study should assess the potential for recovery of impaired microvascular function in collateral-dependent myocardium after recanalization of a CTO, and the determinants of this recovery.
Methods.One-hundred twenty patients underwent a successful recanalization of a CTO (duration>2 weeks), and a follow-up angiography after 5.0±1.2 months. The coronary flow velocity reserve (CFVR) and the fractional flow reserve (FFR) were measured after recanalization, and at follow-up. The global and regional left ventricular (LV) function were analyzed by quantitative angiography.